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Health and Environmental Effects Profile for Methyl Acrylate

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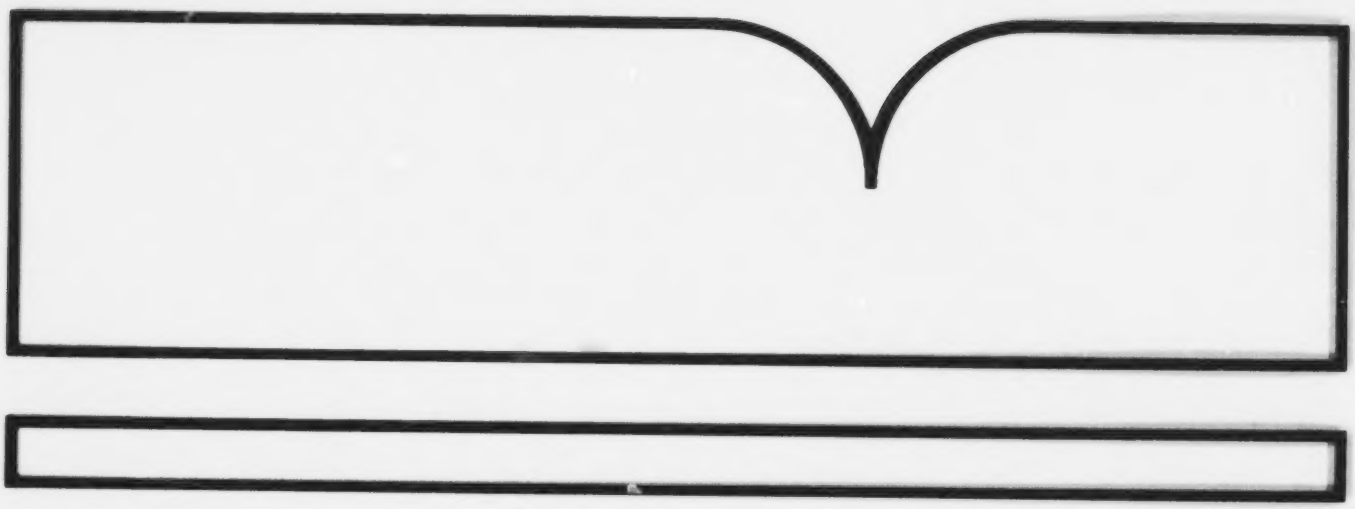

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR METHYL ACRYLATE

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for Methyl Acrylate was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents. Quantitative estimates have been presented provided sufficient data are available. Methyl acrylate has been determined to be a systemic toxicant. A Reference Dose (RfD), defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effect during a lifetime, for methyl acrylate is 0.03 mg/kg/day for oral exposure. The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ value for methyl acrylate is 1000.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1985.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic exposures. An RfD is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, RfDs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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EXECUTIVE SUMMARY

Methyl acrylate is a colorless liquid with an acrid odor (IARC, 1979a). It is reasonably soluble in water and is soluble in a number of organic solvents (Weast, 1985; Windholz, 1983). The chemical is used primarily as a modifying monomer with other acrylates to provide rigidity in resins for leather-finishing, textile and paper coatings, and adhesives; it is also used to produce acrylic fibers and plastic bottles (Celanese Chemical Co., 1981). Currently, two U.S. manufacturers (Badische Corp. and Celanese Chemical Co.) produce methyl acrylate (SRI, 1986). The current U.S. production volume for this chemical is not available.

Methyl acrylate is likely to undergo polymerization if released to the environment in a spill-type situation; however, the diluted concentrations that may be encountered in the environment are unlikely to polymerize significantly. If released to water, volatilization and oxidation by singlet oxygen and hydroxyl radical are expected to be important removal mechanisms. Although methyl acrylate appears to be susceptible to microbial degradation, the quantitative significance of biodegradation in the environment cannot be predicted from the available data. Direct photolysis, adsorption to sediment, bioconcentration and hydrolysis (except if pH $\geq$9) are not expected to be important in water. If released to the atmosphere, methyl acrylate is expected to remain in the vapor phase and react rapidly with HO radical and ozone, with an estimated half-life of 6.5 hours (U.S. EPA, 1986a). If released to soil, methyl acrylate is expected to be highly mobile based on estimated K_{oc} values; therefore, significant leaching in soil may occur. Methyl acrylate may volatilize significantly from soil surfaces. In moist alkaline soil (pH >9), hydrolysis is potentially important.

Pertinent ambient water monitoring data for methyl acrylate could not be located in the available literature as cited in the Appendix. Methyl acrylate was detected in the ambient air near industrial sites in Newark, NJ, at a concentration of 4.545 mg/m^3 and at trace concentrations near industrial sites in Bound Brook, NJ (Pellizzari, 1977). It is possible that methyl acrylate will be emitted to the atmosphere or to water from effluents during its industrial manufacture or use. Leaching of residual monomer from polymer products that have been landfilled may be possible. Since polymer products made from methyl acrylate are permitted for various food contact uses (IARC, 1979b), leaching of residual monomer into foods may be possible. Methyl acrylate has been reported to be a volatile component of pineapple concentrate (IARC, 1979b). Incineration of acrylate polymers may be a source of atmospheric acrylate release. A National Occupational Hazard Survey (NOHS) conducted between 1972 and 1974 estimated that 11,803 U.S. workers are potentially exposed to methyl acrylate (NIOSH, 1984).

The information concerning toxicity of methyl acrylate to aquatic organisms is quite limited. Fish LC_{50} values of 5.0 and 7.5 mg/ℓ were reported by Paulet and Vidal (1975) and Juhnke and Luedemann (1978), respectively. A concentration of 2.4 mg/ℓ caused 52 and 95% mortality of two species of planktonic crustaceans (D'Angelo and Signorile, 1978). The lowest reported toxicity threshold for inhibition of culture growth among three protozoans was 10 mg/ℓ for Chilomonas paramecium (Bringmann and Kuehn, 1981). The most sensitive plant species was the blue-green alga, Microcystis aeruginosa, with a toxicity threshold of 1.3 mg/ℓ (Bringmann and Kuehn, 1978).

Data regarding the rate and extent of absorption of methyl acrylate were not available; however, detection of urinary metabolites or radioactivity following oral and dermal dosing of guinea pigs with unlabeled or ^{14}C-methyl acrylate indicate that the chemical was absorbed by the gastrointestinal tract and skin (Seutter and Rijntjes, 1981). Whole body autoradiography of guinea pigs following oral dosing with ^{14}C-methyl acrylate indicated distribution of radioactivity to the liver, bladder and brain in 2 hours. Autoradiography following dermal application indicated distribution to the heart, lungs and brains. Studies on the metabolism of methyl acrylate in rats demonstrated that conjugation with glutathione to form mercapturic acids and hydrolysis catalyzed by carboxylesterase are competing metabolic pathways (Silver and Murphy, 1981; Delbressine et al., 1981). Guinea pigs treated orally with methyl acrylate excreted ~14% of the dose as thioethers in the urine and an unspecified percentage of the dose in the bile (Seutter and Rijntjes, 1981). Guinea pigs injected intraperitoneally with ^{14}C-methyl acrylate excreted 35.4% of the radioactivity in the expired air as $^{14}CO_2$ in 24 hours. Urinary excretion of radioactivity following oral dosing was 21% in 24 hours and 22.6% in 72 hours.

No carcinogenicity studies of methyl acrylate when the compound was administered orally were available, and this chemical is not scheduled for testing by the National Toxicology Program (NTP, 1987). No evidence of carcinogenicity was found in male or female rats exposed by inhalation to $\leq$135 ppm (475 mg/m^3), 6 hours/day, 5 days/week for up to 2 years (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979).

Methyl acrylate was not found to be genotoxic in reverse mutation assays using S. typhimurium with or without metabolic activation (Waegemaekers and Bensink, 1984; Florin et al., 1980). Ishidate et al. (1981) and Sofuni et

al. (1984a) reported an increase in chromosomal aberrations in a mammalian cell line treated with the ester. Results concerning the mutagenic potential of methyl acrylate in the mouse micronucleus test are equivocal (Przbojewska et al., 1984; Sofuni et al., 1984b). No teratogenicity or reproduction studies were found.

Oral LD_{50} values in experimental animals range from 230-825 mg/kg (Treon et al., 1949; Smyth and Carpenter, 1948; Tanii and Hashimoto, 1982). There are no chronic oral toxicity data for methyl acrylate in experimental animals. A gavage dose of 23 mg/kg methyl acrylate given 24 times over 33 days caused only a minor inhibition of growth in treated rabbits (Treon et al., 1949).

In experimental animals, methyl acrylate was shown to be a potent skin irritant, inducing inflammation, edema and hemorrhaging after dermal application (Treon et al., 1949; Delbressine et al., 1980; Suvorov, 1973; Seutter and Rijntjes, 1981). After 1- to 4-hour inhalation exposure, LC_{50}s range from 1000-33,500 ppm (~3500-118,000 mg/m^3) (Smyth and Carpenter, 1984; Vernot et al., 1977; Lomonova and Klimova, 1979). Signs of intoxication include severe irritation to the mucous membranes and convulsions. Irritation of the nasal mucosa and corneal opacity were observed in rats exposed by inhalation to 15, 45 or 135 ppm (53, 158 or 475 mg/m^3), 6 hours/day, 5 days/week for up to 2 years in a carcinogenesis study (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979). Hematology, urinalysis, and gross and histological examinations revealed no systemic effects.

Exposure of small groups of experimental animals to 107 mg/m^3 methyl acrylate, 7 hours/day for 130 exposures in 185 days led to considerable weight loss in rabbits, guinea pigs and monkeys, but not rats. No other manifestations of toxicity were observed (Treon et al., 1949). Weight loss

was not found in rabbits, guinea pigs or rats exposed to 328 mg/m³, 7 hours/day for 50 days, but rabbits had initial signs of respiratory irritation. At higher concentrations for shorter periods of time, methyl acrylate consistently induced signs of respiratory distress, systemic toxicity and ultimate death. Occupational studies (Suvorov, 1971; Dovzhanskii, 1976; Khromov, 1974) showed that methyl acrylate causes allergic contact dermatitis in man. Application to the rabbit cornea led to a moderately irritating response (Carpenter and Smyth, 1946).

An RfD of 0.03 mg/kg/day or 2 mg/day for a 70 kg man was derived from the NOAEL for systemic toxicity in rats exposed by inhalation to 53 mg/m³, 6 hours/day, 5 days/week for 2 years (converted to 3 mg/kg/day) in the study by Klimisch and Reininghaus (1984) using an uncertainty factor of 100. An RQ of 1000 was derived from the same exposure level at which corneal opacity (considered to be a nonsystemic effect) was observed. Negative results for carcinogenicity in the 2-year inhalation study in rats by Klimisch and Reininghaus (1984) and no data for carcinogenicity in humans constitute inadequate evidence to assess the carcinogenic potential; therefore, methyl acrylate was classified as an EPA Group D chemical (U.S. EPA, 1986b).

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
BOD	Biological oxygen demand
BODT	Biological oxygen demand theoretical
CHL	Chinese hamster lung
CNS	Central nervous system
CS	Composite score
DMSO	Dimethyl sulfoxide
GRAS	Generally recognized as safe
i.p.	Intraperitoneal
K_{oc}	Soil sorption coefficient standardized with respect to organic carbon
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients (and all other subscripted dosage levels)
LD_{50}	Dose lethal to 50% of recipients
LOEL	Lowest-observed-effect level
MED	Minimum effective dose
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
PEL	Permissible exposure level
ppm	Parts per million
PVC	Polyvinyl chloride
RfD	Reference dose
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value

LIST OF ABBREVIATIONS (cont.)

TLV	Threshold limit value
TOTP	Tri-o-tolyl-phosphate
TWA	Time-weighted average
UV	Ultraviolet
WS	Water solubility

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Methyl acrylate is the common name for the compound 2-propenoic acid, methyl ester (current CAS designation), also known as methyl 2-propenoate, methoxycarbonylethylene and acrylic acid, methyl ester. The structure, molecular weight, emipirical formula and CAS number for methyl acrylate are as follows:

Molecular weight: 86.1

Empirical formula: $C_4H_6O_2$

CAS Registry number: 96-33-3

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Methyl acrylate is a colorless liquid with an acrid odor (IARC, 1979b). It is soluble in alcohol, ether, acetone and benzene (Weast, 1985). Selected physical properties are listed below:

Melting point:	below -75°C	Weast, 1985
Boiling point:	79.9°C	Celanese Chemical Co., 1981
Density:	0.9535 (20/4°C)	Weast, 1985
Refractive index:	1.4040 (20°C)	Weast, 1985
Water solubility:		
at 20°C	6 g/100 mℓ water	Windholz, 1983
at 25°C	5.2 g/100 g water	Klein, 1981
Vapor pressure:		
at 9.2°C	40 mm Hg	Perry and Green, 1984
at 17.3°C	60 mm Hg	Perry and Green, 1984
at 20°C	70 mm Hg	Verschueren, 1983
at 28°C	100 mm Hg	Perry and Green, 1984
Log K_{ow}:	0.80	Hansch and Leo, 1985

Vapor density: (air=1.0)	3.0	Verschueren, 1983
Flash point:	-3.3°C (closed cup)	Celanese Chemical Co., 1981
Conversion factors: (air)	1 mg/m³ = 0.28 ppm 1 ppm = 3.5 mg/m³	Verschueren, 1983

Methyl acrylate easily polymerizes on standing (Windholz, 1983); the commercial product may contain from 15-1000 ppm hydroquinone monomethyl ether as an inhibitor (IARC, 1979b). Polymerization is accelerated by heat, light and peroxides (Windholz, 1983). Methyl acrylate is flammable and can be a dangerous fire and explosion hazard (Hawley, 1981).

1.3. PRODUCTION DATA

Commercial production of methyl acrylate was first reported in the United States in 1944 (IARC, 1979b). Production of methyl acrylate in 1976 (excluding any that may have been used to produce higher acrylates) was estimated to have been 4.5 million kg (IARC, 1979b). Recent production figures are not available. In 1984, Celanese Chemical Co. was the only manufacturer reporting production (USITC, 1985). Current U.S. manufacturers of methyl acrylate include Badische Corp., Freeport, TX, and Celanese Chemical Co., Pampa, TX (SRI, 1986). Production data available from the public portion of the U.S. EPA TSCA production file for 1977 (U.S. EPA, 1977) are listed in Table 1-1.

Methyl acrylate is manufactured in the United States by a propylene oxidation process (SRI, 1986). In this process, acrolein is first formed by the catalytic oxidation of propylene vapor at high temperature, which is then oxidized with O_2 to yield acrylic acid (Kine and Novak, 1978). The acrylic acid is then esterified with methanol.

TABLE 1-1

Methyl Acrylate Production Data for 1977*

Producer/Location	Manufacturer or Importer	Production Range (millions of pounds)
Haven Chemical Philadelphia, PA	manufacturer	confidential
Celanese Chemical Co. Pampa, TX	manufacturer	10-50
Miljac Inc. New Canaan, CT	importer	none
Rohm and Haas Co. Philadelphia, PA	importer	1-10

*Source: U.S. EPA, 1977

1.4. USE DATA

Methyl acrylate is used primarily as a modifying monomer with other acrylates to provide rigidity in resins for leather-refinishing, textile and paper coatings and adhesives (Celanese Chemical Co., 1981). It is also used as a component of acrylic fibers and plastic bottles (Celanese Chemical Co., 1981). Small quantities of methyl acrylate are used in the manufacture of amphoteric surfactants (e.g., N-dodecyl-beta-aminopropionic acid) for use in special industrial cleaners and for a variety of other applications (IARC, 1979b).

1.5. SUMMARY

Methyl acrylate is a colorless liquid with an acrid odor (IARC, 1979b). It is reasonably soluble in water and is soluble in a number of organic solvents (Weast, 1985; Windholz, 1983). The chemical is used primarily as a modifying monomer with other acrylates to provide rigidity in resins for leather-finishing, textile and paper coatings, and adhesives; it is also used to produce acrylic fibers and plastic bottles (Celanese Chemical Co., 1981). Currently, two U.S. manufacturers (Badische Corp. and Celanese Chemical Co.) produce methyl acrylate (SRI, 1986). Current U.S. production volume for this chemical is not available.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

Methyl acrylate is subject to polymerization, particularly in the presence of heat or light (Windholz, 1983). Therefore, in a spill-type situation, methyl acrylate may undergo polymerization to a resin form. The fate processes discussed below relate to dilute concentrations of methyl acrylate that may be encountered in the environment; these dilute concentrations are unlikely to experience significant polymerization.

2.1. WATER

2.1.1. Hydrolysis. Hydrolysis rate data of methyl acrylate in the neutral aqueous solution could not be located in the available literature as cited in the Appendix; however, the hydrolysis half-life for ethyl acrylate at 25°C and pH 7 was reported to be 3.5 years (Mabey and Mill, 1978). Based on the acid- and base-catalyzed hydrolysis rate constants reported by Mabey and Mill (1978), hydrolysis of methyl acrylate in environmentally acidic water will be even slower. Hydrolysis in alkaline waters will be faster than at pH 7 and at pH 8 and 25°C, the half-life will be on the order of 100 days; while at pH 9, the half-life will be on the order of 10 days. Roy (1972) reported the alkaline hydrolysis rate constant for methyl acrylate at 25°C to be 0.0779 M^{-1} sec^{-1}, which is very close to the value of 0.078 M^{-1} sec^{-1} for ethyl acrylate reported by Mabey and Mill (1978). Based on the above data, the half-life of methyl acrylate resulting from hydrolysis will be ~10 days at pH 9 and therefore hydrolysis will not be important in most environmental waters. The hydrolysis products, should hydrolysis occur, will be acrylic acid and methanol.

2.1.2. Oxidation. Experimental data specific to the oxidation of methyl acrylate in water could not be located in the available literature as cited in the Appendix; however, oxidation by photochemically produced oxidants,

such as singlet oxygen and HO radical, is potentially an important removal mechanism. The half-life for the reaction of singlet oxygen with unsubstituted or substituted olefins in natural water was reported to be ~7.3-8.0 days (Mill and Mabey, 1985). The reactivity of the acrylate monomers with singlet oxygen in vapor-phase was found to be on the same order of magnitude as reactivity with the olefins (Datta and Rao, 1979). Assuming that reactivity of acrylate monomers and olefins in water is similar, then reaction with singlet oxygen is potentially significant.

The half-life of olefins in water that results from its reaction with HO radical is on the order of 13-14 days (Mill and Mabey, 1985). Since the acrylate monomers contain olefinic double bonds, they may again be susceptible to this oxidation process. Oxidation of olefins with RO_2 radical in water has a reported half-life >200 years (Mill and Mabey, 1985); therefore, this oxidant reaction is not important.

2.1.3. Photolysis. Acetonitrile and both the ethyl and methyl esters of acrylic and methacrylic acids in cyclohexane and methanol, respectively, do not absorb light strongly in the UV spectrum >290 nm (Brunn et al., 1976). This suggests that direct photolysis in water will not be significant compared with its photooxidation by singlet oxygen and HO radical.

2.1.4. Microbial Degradation. Methyl acrylate was confirmed to be significantly biodegradable (bio-oxidation was >30% after 2 weeks of incubation) by the Japanese MITI test (Sasaki, 1978). Thom and Agg (1975) reported that methyl acrylate should be degradable by biological sewage treatment provided suitable acclimatization can be achieved; Speece (1983) suggested that methyl acrylate should be amenable to anaerobic biodegradation for industrial wastewater treatment.

Price et al. (1974) measured the biodegradability of ethyl acrylate using an acclimated and nonacclimated sewage seed in freshwater and non-acclimated sewage seed in synthetic seawater. In all three cases, 20-day BODTs indicated significant bio-oxidation of ethyl acrylate. By analogy, methyl acrylate may also be biodegraded under these test conditions. These data are not sufficient to predict the quantitative significance of methyl acrylate biodegradation in natural water; however, it appears that methyl acrylate may be susceptible to microbial transformation in the natural environment.

2.1.5. **Volatilization.** Based on a vapor pressure of 70 mm Hg (Verschueren, 1983) and a water solubility of 60 g/ℓ (Windholz, 1983) at 20°C, the Henry's Law constant for methyl acrylate can be estimated to be 1.32×10^{-4} atm-m³/mol. This value of Henry's Law constant indicates that volatilization is significant from all environmental waters (Lyman et al., 1982). Using the method of Lyman et al. (1982), the volatilization half-life from a river 1 m deep, flowing at a speed of 1 m/sec, with a wind velocity of 3 m/sec is estimated to be 8.8 hours. The volatilization half-life from a river 10 m deep is estimated to be 7.9 days.

2.1.6. **Adsorption.** Based on a WS of 60 g/ℓ at 20°C (Windholz, 1983) and a log K_{ow} of 0.80 (Hansch and Leo, 1985), partitioning from the water column to particulate organic matter and sediment is not expected to be important.

2.1.7. **Bioconcentration.** The following two equations can be used for estimating the BCF of methyl acrylate (Lyman et al., 1982):

$$\log BCF = 0.76 \log K_{ow} - 0.23 \qquad (2\text{-}1)$$

$$\log BCF = 2.791 - 0.564 \log WS \text{ (water solubility in ppm)} \qquad (2\text{-}2)$$

Based on a log K_{ow} of 0.80 and a WS of 60 g/ℓ at 20°C, the BCF values estimated from Equations 2-1 and 2-2 for methyl acrylate are 2.4 and 1.2, respectively. These values suggest that bioaccumulation of methyl acrylate in aquatic organisms will not be significant.

2.2. AIR

Because of its relatively high vapor pressure, methyl acrylate that is released to the atmosphere is expected to remain in the vapor phase and not become associated with particulate matter.

The rate constants for the vapor-phase atmospheric reaction of methyl acrylate with HO radical and with ozone have been estimated to be 2.7×10^{-11} and 1.3×10^{-17} cm³/molecule-sec, respectively (U.S. EPA, 1986a). Assuming average atmospheric concentrations of 8×10^5 HO radical/m³ and 6×10^{11} O_3 molecules/m³, the half-life of methyl acrylate (with respect to the combined effect of HO radical and O_3) has been calculated to be 6.5 hours (U.S. EPA, 1986a). The half-lives with respect to only HO radical or O_3 can be calculated to be 8.9 and 24.7 hours, respectively.

Since methyl acrylate does not absorb light strongly in the UV region at wavelengths >290 nm (Brunn et al., 1976), direct photolysis is not expected to be significant compared with its reaction to HO radical or ozone.

2.3. SOIL

2.3.1. Microbial Degradation. Pertinent data regarding the microbial degradation of methyl acrylate could not be located in the available literature as cited in the Appendix. Since ethyl and methyl acrylate have been shown to be degradable in various BOD tests (see Section 2.1.4.), microbial degradation in soil may be possible.

2.3.2. Adsorption. K_{oc} values can be estimated using the following two regression equations (Lyman et al., 1982):

$$\log K_{oc} = 3.64 - 0.55 \log WS \text{ (in ppm)} \quad (2\text{-}3)$$

$$\log K_{oc} = 0.544 \log K_{ow} + 1.377 \quad (2\text{-}4)$$

The K_{oc} values calculated from Equations 2-3 and 2-4 for methyl acrylate ($\log K_{ow}$ of 0.80; WS of 60,000 ppm) are 10 and 65, respectively. These estimated K_{oc} values predict high to very high soil mobility (Swann et al., 1983). Therefore, methyl acrylate appears susceptible to significant leaching in soil.

2.3.3. Volatilization. The vapor pressure of methyl acrylate (70 mm Hg at 20°C) indicates that it will volatilize from dry surfaces quite rapidly. In moist soils, volatilization may be significant since methyl acrylate is expected to volatilize from water (see Section 2.1.5.).

2.3.4. Hydrolysis. The hydrolysis of methyl acrylate is not expected to become environmentally important until pH >9 (see Section 2.1.1.). In moist alkaline soils (pH >9), hydrolysis is potentially important for degradation of methyl acrylate.

2.4. SUMMARY

Methyl acrylate is likely to undergo polymerization if released to the environment in a spill-type situation; however, the diluted concentrations that may be encountered in the environment are unlikely to polymerize significantly. If released to water, volatilization and oxidation by singlet oxygen and HO radical are expected to be important removal mechanisms. Although methyl acrylate appears to be susceptible to microbial degradation, the quantitative significance of biodegradation in the environment cannot be predicted from the available data. Direct photolysis, adsorption to sediment, bioconcentration and hydrolysis (except if pH $\geq$9) are not expected to be important in water. If released to the atmosphere,

methyl acrylate is expected to remain in the vapor phase and react rapidly with HO radical and ozone, with an estimated half-life of 6.5 hours (U.S. EPA, 1986a). If released to soil, methyl acrylate is expected to be highly mobile based on estimated K_{oc} values; therefore, significant leaching in soil may occur. Methyl acrylate may volatilize significantly from soil surfaces. In moist alkaline soil (pH >9), hydrolysis is potentially important.

3. EXPOSURE

A National Occupational Hazard Survey conducted between 1972 and 1974 has estimated that 11,803 U.S. workers are potentially exposed to methyl acrylate (NIOSH, 1984).

3.1. WATER

Pertinent aquatic monitoring data for methyl acrylate could not be located in the available literature as cited in the Appendix. The U.S. EPA STORET Data base contained no postings for the compound.

It is possible that methyl acrylate may be discharged with wastewater effluents generated by manufacturing and use operations. Small amounts of residual ethyl acrylate monomer have been found in polymer latexes (IARC, 1979b). Leaching of residual monomer from polymer products that have been landfilled may be possible, although no groundwater monitoring data are available to confirm this suggestion.

3.2. FOOD

Methyl acrylate has been reported to be a volatile component of pineapple concentrate (IARC, 1979b).

The U.S. Food and Drug Administration considers methyl acrylate to be a GRAS (generally recognized as safe) adjuvant in food and polymers, and copolymers made from methyl acrylate are permitted for various contact uses with foods (IARC, 1979b). Residual monomer in these polymers and copolymers may leach into the contacted foods, although data establishing such contamination could not be located in the available literature.

3.3. INHALATION

Methyl acrylate was detected in the ambient air near industrial sites in Newark, NJ, at a concentration of 4.545 mg/m³ and at trace concentrations near industrial sites in Bound Brook, NJ (Pellizzari, 1977). Atmospheric emissions may result from the commercial manufacture and use of methyl acrylate.

The high temperature combustion (>300-800°C) of polydimethacrylates can result in the formation of ethyl methacrylate (Lomakin et al., 1984), suggesting that incineration of methacrylate polymers may produce ethyl methacrylate as a combustion product, which may in turn be released to the atmosphere through stack emission. Incineration of acrylate polymers may therefore be a source of atmospheric release of acrylates.

3.4. DERMAL

Pertinent data regarding dermal exposure of methyl acrylate could not be located in the available literature as cited in the Appendix. Exposure potential may be greatest in occupational settings, and the dermal route leads to systemic uptake (Silver and Murphy, 1981; Delbressine et al., 1981).

3.5. SUMMARY

Pertinent ambient water monitoring data for methyl acrylate could not be located in the available literature as cited in the Appendix. Methyl acrylate was detected in the ambient air near industrial sites in Newark, NJ, at a concentration of 4.545 mg/m³ and at trace concentrations near industrial sites in Bound Brook, NJ (Pellizzari, 1977). It is possible that methyl acrylate will be emitted to the atmosphere or to water from effluents during its industrial manufacture or use. Leaching of residual monomer from polymer products that have been landfilled may be possible. Methyl acrylate has been reported to be a volatile component of pineapple concentrate (IARC,

1979b). Since polymer products made from methyl acrylate are permitted for various food contact uses (IARC, 1979b), leaching of residual monomer into foods may be possible. Incineration of acrylate polymers may be a source of atmospheric acrylate release. A National Occupational Hazard Survey (NOHS) conducted between 1972 and 1974 estimated that 11,803 U.S. workers are potentially exposed to methyl acrylate (NIOSH, 1984).

4. PHARMACOKINETICS

4.1. ABSORPTION

Seutter and Rijntjes (1981) administered 99% pure methyl acrylate by stomach tube to two male guinea pigs at a dose level of 0.40 mmol/kg (34 mg/kg). Five guinea pigs received the same dose of methyl (2,3-^{14}C)-acrylate (specific activity 0.76 mCi/mmol). Any methyl acrylate that remained in the stomach tube was washed down with 0.3 mℓ of 50% ethanol. Urinary thioether concentrations in guinea pigs treated with the unlabeled compound were determined for 24-hour periods, then compared with the baseline concentration. Guinea pigs treated with labeled compound were sacrificed 1, 2, 4, 8 and 16 hours after dosing, sectioned and prepared for whole-body autoradiography.

The urinary elimination of thioether or radioactivity (Sections 4.3. and 4.4.) in guinea pigs treated with unlabeled compound or ^{14}C-methyl acrylate indicated that methyl acrylate was absorbed from the gastrointestinal tract. This conclusion was substantiated by the finding of a distribution of radioactivity throughout body tissues, principally in the liver, bladder and brain, 2 hours after administration.

Seutter and Rijntjes (1981) applied 0.53 mmol/kg (46 mg/kg) methyl acrylate to the shaved skin of eight guinea pigs. Six of the guinea pigs received methyl (2,3-^{14}C)-acrylate and the other two received unlabeled methyl acrylate. The guinea pigs were sacrificed 4, 8, 16, 28 and 40 hours after skin application. For the guinea pigs receiving unlabeled methyl acrylate, urinary thioether levels were measured at three 24-hour intervals. The finding of urinary thioether levels at all three time points in one guinea pig and at one time point in the second guinea pig indicated dermal

absorption; these levels were nonetheless lower than those seen after oral administration (Section 4.4.). For the guinea pigs receiving dermal application of radioactive methyl acrylate, edema was first observed at 4 hours; complete penetration of the dermis was noted at 8 hours, and by 16 hours radioactivity had spread directly into the subcutaneous tissue and the rest of the body.

4.2. DISTRIBUTION

As discussed in Section 4.1., whole-body autoradiography revealed that radioactivity spread into the internal organs, particularly the livers, bladders and brains of guinea pigs 2 hours after oral administration of ^{14}C-methyl acrylate (Seutter and Rijntjes, 1981). Hepatic levels of radioactivity declined gradually and were negligible 16 hours after dosing. Significant retention at 16 hours was found only in the mucosal linings of the stomach, intestines and mouth epithelium. Autoradiography 8-16 hours after dermal application of ^{14}C-methyl acrylate revealed gradual increases of radioactivity in the hearts, lungs and brains of guinea pigs.

Seutter and Rijntjes (1981) also injected six guinea pigs i.p. with 0.40 mmol/kg (34 mg/kg) ^{14}C-methyl acrylate intraperitoneally. Guinea pigs from this group were sacrificed 1, 2, 4, 8, 24 and 48 hours after administration, and their tissues were analyzed by whole-body autoradiography. Radioactivity was concentrated primarily in the liver and peritoneum of the guinea pig sacrificed at 1 hour, but had already started to spread to other organs. Except for the liver and bladder, radioactivity levels decreased in all organs of guinea pigs sacrificed at 2, 4 or 8 hours. The liver and bladder lost their radioactivity only after 24 and 48 hours. At these time points, there was still significant retention in the mucous membranes.

4.3. METABOLISM

Studies on the metabolism of methyl acrylate demonstrate that conjugation with glutathione to form mercapturic acids and hydrolysis by carboxylase activity are competing processes.

Delbressine et al. (1981) treated female Wistar rats intraperitoneally with methyl acrylate in arachis oil at 0.14 mmol/kg/day (12 mg/kg/day), 5 days/week for 3 weeks. Analysis of the urine revealed mercapturic acid formation. The mercapturic acids were identified as N-acetyl-S-(2-carboxyethyl) cysteine as a major component and N-acetyl-S-(2-carboxyethyl) cysteine monomethyl ester as a minor component.

In another experiment Delbressine et al. (1981) treated female adult Wistar rats with 0.14 mmol/kg (12 mg/kg) methyl acrylate in arachis oil by a single i.p. injection in order to quantitate the mercapturic acid formation by measuring urinary thioether excretion. Urine was collected for 24 hours/day for 3 days and analyzed for thioether content. The single dose nearly doubled the amount of thioether excretion over control levels. The investigators also studied the effect of TOTP, a carboxylesterase inhibitor, on the formation of thioesters. When separate groups of rats were pretreated with TOTP, thioether excretion increased dramatically in rats given a single i.p. dose of 12 mg/kg methyl acrylate, but not in the rats injected with the vehicle control. Thin-layer chromatographic analysis revealed that the ratio of excreted N-acetyl-S-(2-carboxyethyl) cysteine to its monomethyl ester was 20:1 without pretreatment, but 1:2 with pretreatment with TOTP.

Silver and Murphy (1981) demonstrated significant hydrolysis of methyl acrylate by lung, kidney and especially liver carboxylesterases in rat tissue homogenates. Pretreatment of rats with 5-125 mg/kg TOTP, 18 hours before inhalation exposure to methyl acrylate, reduced hydrolysis by 38-96% in these tissues and potentiated the toxicity of methyl acrylate.

Pretreatment with 125 mg/kg TOTP, before inhalation exposure to 200-1000 ppm (704-3521 mg/m³) methyl acrylate, also significantly depleted nonprotein sulfhydryl concentrations in rat lungs, blood and liver, an indication that conjugation with glutathione was enhanced. The results of Delbressine et al. (1981) and Silver and Murphy (1981) indicate that the carboxylesterase-mediated hydrolysis is a major detoxification mechanism. When this enzyme is inhibited, however, the pathway of metabolism shifts dramatically toward glutathione conjugation and mercapturic acid (thioether) formation.

4.4. EXCRETION

Following an oral dose of ~34 mg/kg of methyl acrylate to guinea pigs, ~14% of the dose was excreted as thioether (mercapturic acid conjugates) in the urine collected over 72 hours, with ~11% of the dose being excreted in the first 24 hours (Seutter and Rijntjes, 1981). Guinea pigs injected i.p. with 22 mg/kg of methyl(2,3-^{14}C) acrylate excreted 35.4% of the dose of radioactivity in expired air as $^{14}CO_2$ within 24 hours. Total excretion of radioactivity in the urine was 22.6% of the dose in 72 hours, with 21% being excreted in the first 24 hours. Biliary excretion of radioactivity following an oral dose of methyl (2,3-^{14}C) acrylate was substantial within 10 hours, but the amount was not expressed as percentage of dose.

4.5. SUMMARY

Data regarding the extent of absorption of methyl acrylate were not available; however, detection of urinary metabolites or radioactivity following oral and dermal dosing of guinea pigs with unlabeled or ^{14}C-methyl acrylate indicate that the chemical was absorbed by the gastrointestinal tract and skin (Seutter and Rijntjes, 1981). Whole body autoradiography of guinea pigs following oral dosing with ^{14}C-methyl acrylate indicated distribution of radioactivity to the liver, bladder and brain in 2 hours.

Autoradiography following dermal application indicated distribution to the heart, lungs and brains. Studies on the metabolism of methyl acrylate in rats demonstrated that conjugation with glutathione to form mercapturic acids and hydrolysis catalyzed by carboxylesterase are competing metabolic pathways (Silver and Murphy, 1981; Delbressine et al., 1981). Guinea pigs treated orally with methyl acrylate excreted ~14% of the dose as thioethers in the urine and an unspecified percentage of the dose in the bile (Seutter and Rijntjes, 1981). Guinea pigs injected i.p. with ^{14}C-methyl acrylate excreted 35.4% of the radioactivity in the expired air as $^{14}CO_2$ in 24 hours. Urinary excretion of radioactivity following oral dosing was 21% in 24 hours reaching 22.6% in 72 hours.

5. EFFECTS

5.1. CARCINOGENICITY

No carcinogenicity studies by the oral route in animals were located. In a 2-year inhalation study, however, groups of 86 male and 86 female Sprague-Dawley rats were exposed to methyl acrylate vapor at concentrations of 0, 15, 45 or 135 ppm (0, 53, 158 or 475 mg/m^3), 6 hours/day, 5 days/week (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979). Interim kills of 10 rats/sex/group were performed after 12 months and of 15 rats/sex/group after 18 months. The remaining rats were killed after 24 months. At each sacrifice time, gross necropsy and histological examination of unspecified tissues were performed. No evidence of carcinogenicity was found.

Methyl acrylate is not scheduled for testing by the National Toxicology Program (NTP, 1987).

5.2. MUTAGENICITY

Methyl acrylate was negative for reverse mutations in several strains of Salmonella typhimurium with and without metabolic activation (Waegaekens and Bensink, 1984; Florin et al., 1980) (Table 5-1). Methyl acrylate produced chromosomal aberrations in lung fibroblasts in a CHL cell line, as determined by metaphase analysis; a dose of 6.5 µg/mℓ induced aberrations in 20% of cells (Ishidate et al., 1981). Przbojewska et al. (1984) reported dose-related increases in mouse micronucleus assay after injection of 37.5-300 mg/kg of methyl acrylate with significant toxicity evident at 75 mg/kg and higher. As described in abstracts, Sofuni et al. (1984a,b) found that methyl acrylate induced chromosomal aberrations in Chinese hamster cells in culture, but was negative in a mouse micronucleus test.

TABLE 5-1

Mutagenicity Testing of Methyl Acrylate

Assay	Indicator Organism	Purity	Application	Concentration or Dose	Activating System	Response	Comments	Reference
Reverse mutation	Salmonella typhimurium TA98, TA100, TA1537, TA1538, TA1535	>99%	plate incorporation	40-2500 µg/plate	±S-9	-	NC	Waegamaekers and Bensink, 1984
Reverse mutation	S. typhimurium TA100	>99%	liquid suspension	60-600 µg/2 mL incubation medium	±S-9	-	NC	Waegaemaekers and Bensink, 1984
Reverse mutation	S. typhimurium TA98, TA100 TA1535, TA1537	NR	spot test	3 µmol/plate	±S-9	-	NC	Florin et al., 1980
Chromosomal aberration	CHL cells, lung fibroblast line	NR	liquid suspension	various concentrations, but not reported	±S-9	±	6.5 µg/mL, dose at which chromosomal aberrations were detected in 20% of metaphases	Ishidate et al., 1981
Chromosomal aberration	Chinese hamster fibroblasts	NR	vapor phase	189 ppm (666 mg/m³)	none	+	a concentration of 378 ppm (1331 mg/m³) was toxic	Sofuni et al., 1984b
Mouse micronucleus test	mouse bone marrow	NR	inhalation	NR	NA	-	no experimental details reported	Sofuni et al., 1984b
Mouse micronucleus test	F/Balb/c mouse bone marrow cells	NR	i.p. injection of mice	37.5-300 mg/kg	NA	+	dose-related increases in polychromatic erythrocytes with micronuclei at 75 mg/kg lethal to some polychromatic cells	Przbojewska et al., 1984

NC = No comment; NR = not reported; NA = not applicable

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of methyl acrylate could not be located in the available literature as cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding the other reproductive effects of methyl acrylate could not be located in the available literature as cited in the Appendix.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

No chronic oral studies of methyl acrylate were available; however, Treon et al. (1949) orally administered 23 mg/kg methyl acrylate by gavage to two rabbits, 24 times over 33 days. Besides minor growth retardation, there were no changes in the gross or microscopic histopathology of these rabbits.

In the previously described (see Section 5.1.) 2-year inhalation study in which rats were exposed to 0, 15, 45 or 135 ppm (0, 53, 158 or 475 mg/m^3), 6 hours/day, 5 days/week for up to 2 years ophthalmological examinations, hematology and urinalysis tests were also conducted at each sacrifice, in addition to the gross and histological examinations (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979). A temporary decreased body weight gain was observed at 135 ppm. Irritation of the nasal mucosa with atrophy of the neurogenic portion of the olfactory epithelium and proliferation of reserve cells was dose-related. There was also a dose-related corneal opacity and vascularization of the eyes. No signs of systemic toxicity, however, were observed at any exposure level.

Four rabbits, two guinea pigs, two rats and one monkey were exposed to 107 mg/m^3 methyl acrylate, 7 hours/day for 130 exposures in 185 days (Treon et al., 1949). All species except rats showed a substantial weight

loss from exposure. Otherwise, there were no clinical signs, and no effects on formed elements of the blood, clotting times (rabbits) or urinary inorganic:total sulfate ratios (rabbits). There were also no pathological changes in the tissues of affected animals, sacrificed 2 months after the last exposure. No weight losses were observed in four rabbits, two guinea pigs or two rats given 50, 7-hour exposures to 328 mg/m³ methyl acrylate, but the rabbits were found to have slight conjunctival and nasal irritation. Higher exposure concentrations for shorter periods of time (Section 5.6.), were usually lethal.

TSCA-ITC (1985) briefly described a Soviet rat study by Osintseva et al. (1970) involving 100-day inhalation exposure to methyl acrylate. No pathological changes were seen at 0.01 mg/m³, whereas unspecified hemodynamic shifts occurred at 0.1 mg/m³, and reversible structural alterations in various organs were noted at 1 mg/m³. Further details were not available.

5.6. OTHER RELEVANT INFORMATION

Ghanayem et al. (1985) administered methyl acrylate in corn oil by gavage to male F344 rats for analysis of the dose-response and time-course relationships for gastric edema induction. In a preliminary study, a group of eight rats that received 2 mmol/kg (172 mg/kg) methyl acrylate had mucosal congestion, submucosal edema and superficial necrosis of the glandular stomach; the forestomachs were characterized by edema and vacuolization of the tunica muscularis. In separate groups of rats, 2 mmol/kg (172 mg/kg) methyl acrylate produced more severe forestomach edema than did 1 mmol/kg (86 mg/kg), and in the time-course study, a maximum forestomach gravimetric response was obtained 4 hours after 2 mmol/kg oral methyl acrylate. In both the dose-response and the time-course studies, the amount of glandular stomach edema produced was insignificant.

LD_{50} and LC_{50} values of methyl acrylate exposure are summarized in Table 5-2. Lethality after high doses in rabbits was preceded by lethargy and distention of ear veins, tremors, convulsions, running movements, spasms of the diaphragm, labored breathing and cyanosis (Treon et al., 1949). In this study, inhalation exposure of five rabbits, two guinea pigs and two rats to 817 mg/m³ methyl acrylate, 7 hours/day for 11-12 days was lethal to all animals except the two rats. Fassett (1963) characterized unsaturated ester toxicity in man and animals as severely irritating and occasionally lachrymatory. Symptoms after ingestion include collapse, respiratory difficulty and CNS stimulation.

Methyl acrylate has been shown to be a potent skin irritant (Treon et al., 1949; Delbressine et al., 1980; Seutter and Rijntjes, 1981; Suvorov, 1971, 1973; Khromov, 1974; Dovzhanskii, 1976). In rabbits exposed dermally to a total dose of 4.3-32.6 mg/kg, inflammation, intense edema and occasional hemorrhaging were observed (Treon et al., 1949). Microscopic examination of affected skin revealed cloudy swelling of the rete and connective tissue, with scatterings of polymorphonuclear leukocytes and intraepithelial abscesses. Suvorov (1973) noted necrotic and dystrophic changes in the corium, adventitia and epidermis of rabbit skin treated repeatedly with 1% water solutions of methyl acrylate. After 60 days of application, there were increases in serum phosphatase activities, as well as accumulations of mast cells and lymphoid cells in the corium. Seutter and Rijntjes (1981) observed necrosis and edema of the skin of guinea pigs after dermal application of methyl acrylate. Carpenter and Smyth (1946) found methyl acrylate to be moderately irritating to the rabbit cornea after topical administration.

TABLE 5-2

LD_{50} or LC_{50} Values of Methyl Acrylate

Species	Route	LD_{50} or LC_{50}	Reference
Rabbit	oral	~230 mg/kg	Treon et al., 1949
Rat	oral	300 mg/kg	Smyth and Carpenter, 1948
Mouse	oral	825 mg/kg	Tanii and Hashimoto, 1982
Rat	inhalation (4-hour)	1000 ppm (~3500 mg/m³)	Smyth and Carpenter, 1948
Rat	inhalation (1-hour)	~33,500 ppm (~118,000 mg/m³)	Vernot et al., 1977
Rat	inhalation (time NR)	7300 mg/m³	Lomonova and Klimova, 1979
Mouse	inhalation (time NR)	12,800 mg/m³	Lomonova and Klimova, 1979
Rabbit	dermal	1.3 mL/kg (1.2 g/kg)	Smyth and Carpenter, 1948

NR = Not reported

Humans have been shown to suffer a contact dermatitis reaction when exposed to methyl acrylate. Suvorov (1971) reported that 3/57 workers in physical contact with the ester developed occupational dermatitis, which was reversible after washing. Khromov (1974) noted that 76.1% of all workers in contact with methyl acrylate showed a positive intradermal hemagglutination reaction; control data were not provided. Dovzhanskii (1976) observed that acrylates are capable of inducing epidermatitis, contact dermatitis, and, occasionally, eczema. This investigator found that 20% of workers given an epicutaneous drip test with 20 and 50% methyl acrylate were hypersensitive.

5.7. SUMMARY

No oral carcinogenicity studies of methyl acrylate were available, and this chemical is not scheduled for testing by the National Toxicology Program (NTP, 1986). No evidence of carcinogenicity was found in male or female rats exposed by inhalation to $\leq$135 ppm (475 mg/m^3), 6 hours/day, 5 days/week for up to 2 years (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979).

Methyl acrylate was found not to be genotoxic in reverse mutation assays using S. typhimurium with or without metabolic activation (Waegemaekers and Bensink, 1984; Florin et al., 1980). Ishidate et al. (1981) and Sofuni et al. (1984a) reported an increase in chromosomal aberrations in a mammalian cell line treated with the ester. Results concerning the mutagenic potential of methyl acrylate in the mouse micronucleus test are equivocal (Przbojewska et al., 1984; Sofuni et al., 1984b). No teratogenicity or reproduction studies were found.

There are no chronic oral toxicity data for methyl acrylate in experimental animals. A gavage dose of 23 mg/kg methyl acrylate given 24 times over 33 days caused only a minor inhibition in growth in treated rabbits

(Treon et al., 1949). Irritation of the nasal mucosa and corneal opacity were observed in rats exposed by inhalation to 15, 45 or 135 ppm (53, 158 or 475 mg/m^3), 6 hours/day, 5 days/week for up to 2 years (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979). Hematological, urinalysis, gross and histological examinations revealed no systemic effects. Exposure of small groups of experimental animals to 107 mg/m^3 methyl acrylate, 7 hours/day for 130 exposures in 185 days led to considerable weight loss in rabbits, guinea pigs and monkeys, but not rats. No other manifestations of toxicity were observed (Treon et al., 1949). Weight loss was not found in rabbits, guinea pigs or rats exposed to 328 mg/m^3, 7 hours/day for 50 days, but rabbits had initial signs of respiratory irritation. At higher concentrations for shorter periods of time, methyl acrylate consistently induced signs of respiratory distress, systemic toxicity and ultimate death.

Oral LD_{50} values in experimental animals range from 230-825 mg/kg (Treon et al., 1949; Smyth and Carpenter, 1948; Tanii and Hashimoto, 1982). After 1- to 4-hour inhalation exposure, LC_{50}s range from 1000-33,500 ppm (~3500-118,000 mg/m^3) (Smyth and Carpenter, 1984; Vernot et al., 1977; Lomonova and Klimova, 1979). Signs of intoxication include severe irritation to the mucous membranes and convulsions. In experimental animals, methyl acrylate was shown (Treon et al., 1949; Delbressine et al., 1980; Suvorov, 1973; Seutter and Rijntjes, 1981) to be a potent skin irritant, inducing inflammation, edema and hemorrhaging after dermal application. Occupational studies (Suvorov, 1971; Dovzhanskii, 1976; Khromov, 1974) showed that methyl acrylate causes allergic contact dermatitis in man. Application to the rabbit cornea led to a moderately irritating response (Carpenter and Smyth, 1946).

6. AQUATIC TOXICITY

6.1. ACUTE

Little information is available concerning toxicity of methyl acrylate to fish and aquatic invertebrates. Juhnke and Luedemann (1978) determined the 48-hour LC_{50} for the golden orfe, Leuciscus idus, to be 7.5 mg/ℓ. LC_0 and LC_{100} values were 5 and 10 mg/ℓ, respectively. Paulet and Vidal (1975) reported a 3-day LC_{50} of 5 mg/ℓ for an unspecified fish species.

D'Angelo and Signorile (1978) found that 96 hours of exposure to 2.4 mg/ℓ caused 95 and 52% mortality of the planktonic crustaceans, Moina macrocopa and Cypria ophthalmica, respectively. Bringmann and Kuehn (1981) determined toxicity thresholds for inhibition of culture growth for three protozoan species. These values were 64 mg/ℓ for Uronema parduczi, 11 mg/ℓ for Entosiphon sulcatum and 10 mg/ℓ for Chilomonas paramecium.

6.2. CHRONIC

Pertinent data regarding the chronic toxicity of methyl acrylate could not be located in the available literature as cited in the Appendix.

6.3. PLANTS

Bringmann and Kuehn (1977, 1978) determined toxicity thresholds for inhibition of culture growth of certain algae and bacteria. Toxicity thresholds were 1.3 mg/ℓ for the blue-green alga, Macrocystis aeruginosa, 7.0 mg/ℓ for the green alga, Scenedesmus quadricauda, and 100 mg/ℓ for the bacterium, Pseudomonas putida.

6.4. RESIDUES

Pertinent data regarding the methyl acrylate residues in aquatic biota could not be located in the available literature as cited in the Appendix.

6.5. SUMMARY

The information concerning toxicity of methyl acrylate to aquatic organisms is quite limited. Fish LC_{50} values of 5.0 and 7.5 mg/ℓ were reported by Paulet and Vidal (1975) and Juhnke and Luedemann (1978), respectively. A concentration of 2.4 mg/ℓ caused 52 and 95% mortality of two species of planktonic crustaceans (D'Angelo and Signorile, 1978). The lowest reported toxicity threshold for inhibition of culture growth among three protozoans was 10 mg/ℓ for Chilomonas paramecium (Bringmann and Kuehn, 1981). The most sensitive plant species was the blue-green alga, Microcystis aeruginosa, with a toxicity threshold of 1.3 mg/ℓ (Bringmann and Kuehn, 1978).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The ACGIH (1985-1986) adopted a TLV-TWA of 10 ppm (~35 mg/m^3) for methyl acrylate. In their latest documentation, the ACGIH (1986) cited work of prior investigators (Treon et al., 1949; Smyth, 1955), suggesting that 10 ppm should be a threshold limit for lacrimatory and other primary irritant effects. A "skin" designation was added to the TLV-TWA because of the ester's irritancy effects. The OSHA PEL is also 10 ppm with a "skin" designation (OSHA, 1985).

The U.S. FDA (1983) did not affirm methyl acrylate as a GRAS indirect human food ingredient. This agency could not find evidence that the ester was used in the manufacture of food-related paper and paperbound products, except as a component of polymers already regulated by current and prior food additive restrictions.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic biota from the effects of methyl acrylate could not be located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

No oral carcinogenicity studies of methyl acrylate were available, and this chemical is not scheduled for testing by NTP (1987). No evidence of carcinogenicity was found in male or female rats exposed by inhalation to ≤135 ppm (475 mg/m³), 6 hours/day, 5 days/week for up to 2 years (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979).

Methyl acrylate was found not to be genotoxic in reverse mutation assays using S. typhimurium with or without metabolic activation (Waegemaekers and Bensink, 1984; Florin et al., 1980). Ishidate et al. (1981) and Sofuni et al. (1984a) reported an increase in chromosomal aberrations in a mammalian cell line treated with the ester. Results concerning the mutagenic potential of methyl acrylate in the mouse micronucleus test are equivocal (Przbojewska et al., 1984; Sofuni et al., 1984b). No teratogenicity or reproduction studies were found.

There are no chronic oral toxicity data for methyl acrylate in experimental animals. A gavage dose of 23 mg/kg methyl acrylate given 24 times over 33 days caused only a minor inhibition of growth in treated rabbits (Treon et al., 1949). Irritation of the nasal mucosa and corneal opacity were observed in rats exposed by inhalation to 15, 45 or 135 ppm (53, 158 or 475 mg/m³), 6 hours/day, 5 days/week for up to 2 years (Klimisch and Reininghaus, 1984; Klimisch and Zeller, 1979). Hematological, urinalysis, gross and histological examinations revealed no systemic effects. Exposure of small groups of experimental animals to 107 mg/m³ methyl acrylate, 7 hours/day for 130 of 185 days led to considerable weight loss in rabbits, guinea pigs and monkeys but not rats. No other manifestations of toxicity were observed (Treon et al., 1949). Weight losses were not found in

rabbits, guinea pigs or rats exposed to 328 mg/m³, 7 hours/day for 50 days, but rabbits had initial signs of respiratory irritation. At higher concentrations for shorter periods of time, methyl acrylate consistently induced signs of respiratory distress, systemic toxicity and death.

In the absence of oncogenicity data, it is appropriate to derive an RfD (formerly called ADI). The repeated oral dosing study (rabbits) by Treon et al. (1949) suggests a NOAEL at a TWA dose of 16.7 mg/kg/day (23 mg/kg x 24/33 days); however, the small sample size used and short exposure duration make the use of this study inappropriate in quantitative risk assessment.

In the 2-year inhalation study using rats, no evidence of systemic toxicity was observed at exposures of 15, 45 or 135 ppm (53, 158 or 475 mg/m³), 6 hours/day, 5 days/week (Klimisch and Reininghaus, 1984). The only effects were dose-related irritation of the nasal mucosa and corneal opacity. Since these effects are a direct consequence of exposure to the vapor they would not be expected to occur after ingestion. The exposures can be converted to equivalent oral doses by multiplying by 6 hours/24 hours, 5 days/7 days, by 0.223 m³/day (the reference breathing rate of a 0.35 kg rat), by 0.5 (the absorption factor) and by dividing by 0.35 kg. Thus, the 53, 158 and 475 mg/m³ levels are equivalent to 3, 9 and 27 mg/kg/day, respectively. These doses could be considered NOELs for oral exposure; however, Treon et al. (1949) reported weight loss in rabbits, guinea pigs and monkeys exposed to 107 mg/m³, 7 hours/day for 130 exposures in 185 days. The exposure can be converted to equivalent doses by multiplying by 7 hours/24 hours, by 130/185 days, by 0.5 (absorption factor), by the animal breathing volumes of 2.0 m³/day for rabbits, 0.40 m³/day for guinea pigs and 5.4 m³/day for monkeys (U.S. EPA, 1985), and

dividing by the animal body weights of 3.8 kg for rabbits, 0.84 kg for guinea pigs and 8.0 kg for monkeys. The doses, thus calculated are: 6 mg/kg/day for rabbits, 5 mg/kg/day for guinea pigs and 7 mg/kg/day for monkeys. These doses can be considered LOAELs; therefore, the exposure of 53 mg/m^3, 6 hours/day, 5 days/week for 2 years, equivalent to 3 mg/kg/day, is the highest NOEL below which there is no LOAEL (Klimisch and Reininghaus, 1984). Dividing by an uncertainty factor of 100 (10 for interspecies extrapolation and 10 to protect sensitive individuals) yields an RfD of 0.03 mg/kg/day or 2 mg/day for a 70 kg man.

9. REPORTABLE QUANTITY

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

No chronic or subchronic oral studies of methyl acrylate were located, but one subchronic and one chronic inhalation study was available. These studies were discussed in Section 5.5. and are summarized in Table 9-1. In the presence of the well-conducted chronic study by Klimisch and Reininghaus (1984), the subchronic study by Treon et al. (1949) will not be considered for RQ derivation. Furthermore, the subchronic study used very small numbers of animals.

The only effects observed in the rats exposed to methyl acrylate vapors for 2 years were dose-related irritation of the nasal mucosa with atrophy of the epithelium and proliferation of reserve cells, which would warrant an RV_e of 4, and dose-related corneal opacity and eye vascularization, which would warrant an RV_e of 7. Multiplying the lowest transformed dose at which these effects occurred (6 mg/kg/day) by the cube root of the ratio of the rat body weight to the human body weight (70 kg) and by 70 kg results in an MED of 71.8 mg/day, which corresponds to an RV_d of 2.7 (Table 9-2). Multiplying the RV_d by the higher RV_e of 7 yields a CS of 19, which corresponds to an RQ of 1000 (Table 9-3).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Klimisch and Reininghaus (1984) found no evidence of carcinogenicity in groups of 86 male and 86 female rats exposed to methyl acrylate vapor at 53, 158 or 475 mg/m³, 6 hours/day, 5 days/week for up to 2 years. No other information regarding the carcinogenicity of methyl acrylate to animals was available. Existing animal data are not adequate to evaluate the carcinogenic potential of methyl acrylate. Since no data regarding the carcinogenicity to humans were available, methyl acrylate is classified as an EPA Group D chemical (U.S. EPA, 1986b).

TABLE 9-1

Inhalation Toxicity Summary for Methyl Acrylate[a]

Species/ Strain	Sex	No. at Start	Average Weight[b] (kg)	Vehicle/ Physical State	Exposure	Transformed Animal Dose[c] (mg/kg/day)	Response	Reference
Rat/ Sprague-Dawley	M,F	86/sex/ group	0.35	vapor	15, 45 or 135 ppm (53, 158 or 475 mg/m³), 6 hours/day, 5 days/week for 2 years	6.0, 18.1 or 54.3	Dose-related irritation of nasal mucosa with atrophy of olfactory epithelium and proliferation of reserve cells; dose-related corneal opacity and vascularization of the eyes	Klimisch and Reininghaus, 1984
Rabbit/NR	NR	4	3.8	vapor	107 mg/m³, 7 hours/day for 130 exposures in 185 days	11.5	weight loss	Treon et al., 1949
Guinea pig/NR	NR	2	0.84	vapor	107 mg/m³, 7 hours/day for 130 exposures in 185 days	10.4	weight loss	Treon et al., 1949
Monkey/NR	NR	1	8.0	vapor	107 mg/m³, 7 hours/day for 130 exposures in 185 days	14.8	weight loss	Treon et al., 1949

[a]Purity of compound was not reported

[b]Reference weights from U.S. EPA (1985)

[c]Calculated by expanding the exposure over 24 hours and over 7 days/week or 185 days, by multiplying by the animal breathing rates of 0.223 m³/day for rats, 2.0 m³/day for rabbits, 0.40 m³/day for guinea pigs and 5.4 m³/day for monkeys (U.S. EPA, 1985) and dividing by the animal body weight

NR = Not reported

TABLE 9-2

Inhalation Composite Scores for Methyl Acrylate Using Rat Data*

Animal Dose (mg/kg/day)	Chronic Human MED (mg/day)	RV_d	Effect	RV_e	CS	RQ
6	71.8	2.7	corneal opacity	7	19	1000

*Source: Klimisch and Reininghaus, 1984

TABLE 9-3

Methyl Acrylate

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	inhalation
Dose*:	71.8
Effect:	corneal opacity
Reference:	Klimisch and Reininghaus, 1984
RV_d:	2.7
RV_e:	7
Composite Score:	19
RQ:	1000

*Equivalent human dose

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

GLOBAL
TSCATS
CASR online (U.S. EPA Chemical Activities Status Report)
CAS online STN International
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register

These searches were conducted in April, 1986. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

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Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

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